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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,662	05/24/2001	Toyoki Moribe	0032-0261P	3176

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EXAMINER	
CLOW, LORI A	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 11/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,662	MORIBE ET AL.	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- Th MAILING DATE of this communication app ars on th cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' arguments, filed 20 August 2003, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-8 are currently pending.

Objections to the Claims

Claims 1 and 8 are objected to because of the following informalities:

Claim 1 recites at step (f) "the signal pattern detected at the step (e)". Please delete "the step" and replace with "step".

Claim 8 recites a myriad of SEQ ID NOS that were not elected. The claim should be amended to reflect the elected sequence.

Appropriate correction is required.

Drawings

Applicant is kindly requested to re-submit the drawings 1-6. In the transition from paper files to image file wrappers, the drawings have been either lost or misplaced.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 still recites step (f) to determine the type of the HLA class I allele based on the signal pattern according to the Typing Table. However, a typing table is described only briefly on page 6 and it is unclear from the explanation where to find what table to use. Are patterns compared to known HLA alleles so that a comparison can be made or are the patterns compared to known tables? If the tables are "known" tables, which ones are they and/or where are they found?

Claim 1 recites the limitation "the Typing Table" in step (f). There is insufficient antecedent basis for this limitation in the claim.

Claim 3 is still unclear as to what is meant by "adding an enzyme-conjugate which specifically **bonds** to the label thereto at the same time as or after hybridization". Does Applicant mean "adding an enzyme-conjugate which specifically **binds** to the labeled products during or after hybridization"?

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-4 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawai et al (Human Immunology (1994) Vol. 41, pages 121-126) in view of GenBank Accession Number X97645 (2 December 1996), in view of Tokunaga et al. (Human Immunology (1996) Vol.47, abstract P561, page 103), in further view of Olejnik et al. (Nucleic Acids Research (1998) Vol. 26, pages 3572-3576).

Applicant's arguments with respect to claims 1-8 have been considered but are moot in view of the new ground(s) of rejection. Arguments as they pertain to the amended claims are addressed below.

As stated in the prior Office Action, the present invention requires HLA class I allele typing by amplifying HLA-A, B, and C alleles with PCR primers, adding amplified products to microtiter plates that contain modified DNA probes, detecting signals, and determining an HLA typing pattern. This is further defined by requiring label of the primer pairs, addition of an enzyme-conjugate to bind probe labels, adding chromogenic, luminescent, or fluorescent substrate. Furthermore, one primer pair may be biotinylated and the enzyme may be streptavidin, hybridization is performed in a solution containing formamide and at a room temperature, and the probes can specifically hybridize with a specific HLA allele (in this case SEQ ID NO:3).

Kawai et al. teach a method for HLA typing called microtiter plate hybridization (MPH). In this method, single stranded oligonucleotides are immobilized on a microtiter plate and target

DNA that has been PCR amplified with biotinylated primers are hybridized. The bound DNA is detected colorimetrically by means of biotin-streptavidin methods (see page 122, 1st paragraph).

Kawai et al. do not teach the specific allele of SEQ ID NO:3, as in claim 8. However, GenBank Accession Number X97645 does. This sequence allele is contained in the *B.Taurus* MHC class I gene, exon 2, containing 349 base pairs. The allele within this sequence span stretches from nucleic acid 79-97, matching 100% the allele sequence SEQ ID NO:3.

While Kawai et al. does not teach the use of this method for class I allele typing and does not teach the specific use of SEQ ID NO:3, Tokunaga et al. does teach MPH typing for the alleles of HLA-A, B, and C (see p561 abstract). It would have been prima facie obvious to one of ordinary skill in the art to utilize known alleles of MHC class I for primer and probe design in effort to type all polymorphisms in these loci, the motivation provided by Kawai et al. in stating that the method will be useful for typing other HLA subtypes (see discussion). SEQ ID NO: 3 is in the MHC class I loci and would be useful for probe and primer design to use in the MPH method.

Kawai et al. do not teach the amino modification of DNA probes, however Olejnik et al. do teach this limitation. They state that amino-modified oligonucleotides can be used for preparation of affinity matrices and as immobilized PCR primers. They specifically describe an aminotag for probe design (see page 3572, introduction). The motivation to amino modify the probes of the instant invention is clear in that Olejnik et al. state that the aminotags provide expanded applications for any marker or tag introduced into DNA or RNA (see discussion).

Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawai et al. (Human Immunology (1994) Vol. 41, pages 121-126) in view of GenBank Accession Number X97645 (2 December 1996), in view of Tokunaga et al. (Human Immunology (1996) Vol.47, abstract P561, page 103), in further view of Olejnik et al. (Nucleic Acids Research (1998) Vol. 26, pages 3572-3576) as applied to claims 1-4 and 8 above and in further view of Kox et al. (Journal of Clinical Microbiology (1996) Vol. 34, pages 2117-2120).

Kawai et al. do not teach the specific hybridization conditions used in the method. However, Kox et al. teach a microwell hybridization assay that includes a hybridization reaction in the presence of formamide at 37 degrees, followed by a wash a room temperature, meeting the limitations of claims 5-7 (page 2118, column 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to use the hybridization method of Kawai et al. to type HLA class I alleles A, B, and C, as done by Tokunaga et al. The motivation to do so is provided by Kawai et al. in the discussion section where they state "We believe that PCR-MPH could replace conventional LCT for routine DR typing. This method may be well suited for the automation of HLA typing". Furthermore, as stated above the specific hybridization conditions were well known in the art, as shown by Kox et al. and it would have been prima facie obvious to use these conditions for the optimization of the hybridization reaction.

Response to Arguments

Applicant argues that the references do not teach a method wherein a typing table is generated based upon signal patterns. This is not persuasive in that the current claims do not

require that a typing table be generated based upon signal patterns. Rather, a typing table is used to identify the type of HLA class I allele. Furthermore, Kawai et al., at page 124, column 2, third paragraph show that patterns were analyzed and compared with generated data from serologic or other methods. Kawai et al. also generate a table of absorbance values representative of the DRB1 allele type, similar to the tables listed in the instant specification.

Applicant further argues that a PCR-based method for HLA class I typing had been remarkably delayed and difficult to develop. This is not persuasive, in that Tokunaga et al. clearly states that HLA class I alleles (A, B, and C) were typed using a MPH method, as set forth above.

Applicant argues that Tokunaga et al. do not state whether or not PCR-SSOP is used for HLA class I typing. This is not persuasive in that Tokunaga et al. clearly state that "alleles of HLA A, B, and C were determined using PCR-SSOP and MPH".

No claims are allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

Lori A Clow
AU 1631

MARJORIE MORAN
PATENT EXAMINER

Marjorie A. Moran